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EXAMINER
RUSSEL, J

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DATE MAILED: 01/19/95

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined ☐ Responsive to communication filed on _____ ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), _____ days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☒ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice of Draftsman's Patent Drawing Review, PTO-948.
3. ☒ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____.

Part II SUMMARY OF ACTION

1. ☒ Claims 1-21 are pending in the application.

   Of the above, claims _____ are withdrawn from consideration.

2. ☐ Claims _____ have been cancelled.

3. ☐ Claims _____ are allowed.

4. ☒ Claims 1-21 are rejected.

5. ☐ Claims _____ are objected to.

6. ☐ Claims _____ are subject to restriction or election requirement.

7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.

8. ☐ Formal drawings are required in response to this Office action.

9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice of Draftsman's Patent Drawing Review, PTO-948).

10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____. has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).

11. ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).

12. ☐ Acknowledgement is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____ ; filed on _____.

13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.

14. ☐ Other

EXAMINER'S ACTION

1. The oath or declaration is defective. A new oath or declaration in compliance with 37 C.F.R. § 1.67(a) identifying this application by its Serial Number and filing date is required. See M.P.E.P. §§ 602.01 and 602.02.

The oath or declaration is defective because:

Non-initialed and/or non-dated alterations have been made to the oath or declaration (see 37 C.F.R. §§ 1.52(c) and 1.57 and MPEP 605.05). Note the white-out correction to the city of residence and the correction to the citizenship of Inventor Olejnik.

2. The disclosure is objected to because of the following informalities: At page 1, line 12, "is" should be changed to "are". Appropriate correction is required.

3. Claims 1-4, 7, 8, 13-16, and 18-21 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The word "stable" at claim 1, line 1, is indefinite because "stable" is a relative term, but no point of reference has been given with which to determine whether a particular composition is "stable" or not and therefore embraced within the scope of the claims. The term is defined neither in the claims, the specification, nor the art. Note that a lack of crystallization for a period of up to about nine months, while an example of stability, does not appear to be the definition of stability because otherwise dependent claim 9 would not further limit independent claim 1 under 35 U.S.C. 112, fourth paragraph. At claim 3, line 2; claim 4, line 2; claim 7, line 2; and claim 13, line 2; "a" should be changed to "the". In claims 3, 7, and 13, either "between" should be changed to "from" or else "to" (last occurrence in each claim) should be changed to "and". Compare claim 15 for the proper idiomatic usage of

"between". Claim 4 specifies a weight ratio of cyclosporin to castor oil, but none of the claims upon which claim 4 depends requires that castor oil be present in the composition. Should claim 4 be interpreted as requiring that the higher fatty acid glyceride comprise castor oil, or should claim 4 be amended so that "castor oil" is changed to "higher fatty acid glyceride"? Claim 4 recites that the ratio of cyclosporin to castor oil is below about 0.16 (i.e. there is significantly less cyclosporin than castor oil). However, claims 8, 14, and 15 recite that the ratio of castor oil to cyclosporin is below 0.16 (i.e. that there is significantly less castor oil than cyclosporin). It is unlikely that Applicants intended for both these ratios to be specifically claimed, especially as Example 1 of the specification discloses only compositions embraced by the ratio range of claim 4. Compare also page 6, lines 6-7 and 9-10. At claim 16, line 3, the phrase "poor water solubility" is indefinite because "poor" is a relative term, but no point of reference has been given with which to determine whether a particular active agent has "poor" water solubility or not and therefore whether the particular active agent is embraced within the scope of the claims. The term is defined neither in the claims, the specification, nor the art. At claim 20, lines 2-3, "a" should be changed to "the" and "essentially" should be deleted so that standard Markush language is used. See MPEP 706.03(y). Otherwise, it is not clear what constitutes all of the members of the Markush group. Claim 21, which is dependent upon claim 16, requires sufficient higher fatty acid glyceride and polysorbate 80 to prevent crystallization of cyclosporin for up to about nine months. However, independent claim 16 recites

that an active agent having poor water solubility, and not necessarily cyclosporin, is present in the composition. Accordingly, it is not clear if claim 21 should be interpreted as requiring the presence of cyclosporin in the composition.

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

For the purposes of this invention, the level of ordinary skill in the art is deemed to be at least that level of skill demonstrated by the patents in the relevant art. Joy Technologies Inc. v. Quigg, 14 USPQ2d 1432 (DC DC 1990). One of

ordinary skill in the art is held accountable not only for specific teachings of references, but also for inferences which those skilled in the art may reasonably be expected to draw. In re Hoeschele, 160 USPQ 809, 811 (CCPA 1969). In addition, one of ordinary skill in the art is motivated by economics to depart from the prior art to reduce costs consistent with desired product properties. In re Clinton, 188 USPQ 365, 367 (CCPA 1976); In re Thompson, 192 USPQ 275, 277 (CCPA 1976).

5. Claims 1-3, 9-11, 16, 17, and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Hewitt et al in view of Hackh's Chemical Dictionary. Hewitt et al teach pharmaceutical compositions comprising 0.2-25% cyclosporin A, 5-60% or 5-80% olive oil, and 0.2-20% polysorbate-80. See, e.g., column 4, lines 16-39. Hackh's Chemical Dictionary teaches that olive oil is inherently comprised of higher fatty acid glycerides, e.g., olein and palmitin. Because the compositions are the same, those of Hewitt et al would have been expected to be stable and to avoid crystallization of cyclosporin to the same extent claimed by Applicants.

6. Claims 4-8 and 12-15 are rejected under 35 U.S.C. 103 as being obvious over Hewitt et al in view of Hackh's Chemical Dictionary as applied against claims 1-3, 9-11, 16, 17, and 21 above, and further in view of Kaswan. Hewitt et al do not teach the use of castor oil in their compositions, although Hewitt et al disclose generally the use of solvents, diluents, and carriers such as olive oil, mineral oils, petroleum derivatives, and cetyl and steryl alcohols (see, e.g., claim 7). Kaswan disclose that castor oil is a known pharmaceutically acceptable excipient for use in cyclosporins and is functionally equivalent to olive oil,

mineral oil, petroleum jelly, and alcohol excipients. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to use as the pharmaceutical carrier of Hewitt et al and to substitute for the olive oil component of Hewitt et al's specific compositions the castor oil excipient disclosed by Kaswan, because Hewitt et al's cyclosporin-containing compositions are not limited to any specific solvents, diluents, and carriers, because Kaswan discloses castor oil to be a known excipient for cyclosporin-containing compositions, and because it would have been prima facie obvious to substitute known functionally equivalent components, i.e. olive oil and castor oil, for one another.

7. Claims 16, 18, and 20 are rejected under 35 U.S.C. 102(b) as being anticipated by Hollingsbee. Hollingsbee teaches emulsions comprising dexamethasone in castor oil and Tween 80. See, e.g., Examples 3 and 4. Any steroid can be used, including prednisolone and prednisolone acetate. See, e.g., column 5, lines 2-10.

8. Claims 1-3, 9-11, and 16-21 are rejected under 35 U.S.C. 103 as being obvious over Benita et al. Benita et al disclose emulsions comprised of hydrophobic drugs such as indomethacin, steroids such as protestosterone and testosterone propionate (which are androgens), and cyclosporin; a vegetable oil such as soybean oil, cotton seed oil, olive oil, and sesame oil, which inherently contain higher fatty acid glyceride; and a surfactant such as polysorbate 80. See, e.g., column 3, lines 56-58; column 4, lines 11-27; column 5, lines 1-5; and claims 16, 19, and 25. Benita et al do not teach Applicants' specifically claimed combinations of hydrophobic drugs, higher fatty acid glyceride-

containing vegetable oil; and polysorbate 80. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to form emulsions comprised of each of the hydrophobic drugs, vegetable oils, and surfactants specifically disclosed by Benita et al because Benita et al disclose that each of the specific examples is useful in forming pharmaceutical compositions and because disclosure of the generic compositions renders prima facie obvious the specific compositions encompassed within the genus. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to determine all operable and optimal proportions of components in the emulsions of Benita et al because it is routine in the art to determine such proportions in the pharmaceutical art.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey E. Russel at telephone number (703) 308-3975. The examiner can normally be reached on Monday-Thursday from 8:30 A.M. to 6:00 P.M. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill Warden, can be reached at (703) 308-4037. The fax number for Group 180 is (703) 308-4227 and the telephone number for the Group 180 receptionist is (703) 308-0196.

Jeffrey E. Russel
Primary Patent Examiner
Art Unit 1811

JRussel
January 18, 1995